

What is claimed is:

*Sub D1*  
~~1. A ligand less than about 6 kDa, which binds to a polypeptide comprising the amino acid sequence GWGQPHGG (SEQ ID NO:1) or a polypeptide analog comprising amino acid analogs that are retro-inverso isomers of the amino acid sequence GWGQPHGG (SEQ ID NO:1).~~

2. The ligand of claim 1, wherein said ligand is less than about 4 kDa.

~~3. The ligand of claim 1, wherein said ligand is a nucleic acid or nucleic acid analog.~~

~~4. The ligand of claim 1, wherein said ligand is a carbohydrate.~~

5. The ligand of claim 1, wherein said ligand is a peptide or peptidomimetic.

~~6. The ligand of claim 1, wherein said ligand includes a moiety selected from the group consisting of a porphyrin ring, a phthalocyanine, a naphthoquinone, an imidazole, a purine, or a pyrimidine.~~

7. The ligand of claim 1, wherein said ligand is a peptide ligand less than 20 amino acids in length.

8. The peptide ligand of claim 7, wherein said polypeptide comprises the amino acid sequence GWGQPHGGGWGQPHGG (SEQ ID NO:2).

*Sub D2*  
*Sub A1*  
9. The peptide ligand of claim 7, wherein said polypeptide comprises a retro-inverso isomer of the amino acid sequence D(GGHPQGWG) (SEQ ID NO:39).

10. The peptide ligand of claim 7, wherein the amino acid sequence of said peptide ligand is not present in a streptavidin polypeptide.

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11. The peptide ligand of claim 7, wherein said peptide ligand binds to said polypeptide in the presence of a metal.

12. The peptide ligand of claim 11, wherein said metal is copper.

13. The peptide ligand of claim 12, wherein copper is present at a concentration from about 100 nM to about 500  $\mu$ M.

14. The peptide ligand of claim 12, wherein copper is present at a concentration from about 500 nM to about 200  $\mu$ M.

15. The peptide ligand of claim 7, wherein said peptide ligand includes the amino acid sequence  $X_1X_2X_3X_4X_5X_6$ , provided that

$X_1$  is L, W, or I;

$X_2$  is L, Q, F, or L;

$X_3$  is I, Y, V, F, or L;

$X_4$  is W or V;

$X_5$  is I; and

$X_6$  is P, A, F, K, or A.

~~16. The peptide ligand of claim 15, wherein said peptide ligand comprises an amino acid sequence selected from the group consisting of LLIWIP (SEQ ID NO:3), WLYWIP (SEQ ID NO:4), WL VWIA (SEQ ID NO:27), IQIWIF (SEQ ID NO:21), IFFWIK (SEQ ID NO:23), and LLLVIA (SEQ ID NO:13).~~

~~17. The peptide ligand of claim 7, wherein said peptide ligand comprises the amino acid sequence of a peptide of Table 1 (SEQ IDs 3-30).~~

18. The peptide ligand of claim 7, wherein said peptide ligand is less than 15 amino acids in length.

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19. A polypeptide comprising the amino acid sequence of two or more of the peptide ligands of claim 7.

20. A composition comprising the peptide ligand of claim 7.

21. The composition of claim 20, wherein said composition comprises a solid support.

22. The composition of claim 21, wherein said peptide ligand is coupled to said solid support.

23. The composition of claim 22, wherein said solid support is a resin.

24. The composition of claim 22, wherein said solid support is a membrane.

25. A composition comprising the polypeptide of claim 19.

26. The composition of claim 25, wherein said composition comprises a solid support.

27. The composition of claim 26, wherein said peptide is coupled to said solid support.

28. The composition of claim 27, wherein said solid support is a resin.

29. The composition of claim 27, wherein said solid support is a membrane.

30. A method of identifying a ligand for a prion protein, the method comprising:

- a) contacting a test agent with a peptide comprising at least four continuous amino acids of the sequence GWGQPHGGGWGQPHGG (SEQ ID NO:2), or at least four continuous monomers of or a polypeptide analog comprising amino acid analogs that are retro-inverso isomers of the amino acid sequence GWGQPHGG (SEQ ID NO:1); and
- b) detecting a complex comprising the test agent and said polypeptide, thereby identifying a ligand for a prion protein.

31. The method of claim 30, wherein the peptide comprises at least five continuous amino acids of the sequence GWGQPHGGGWGQPHGG (SEQ ID NO:2).
32. A method of identifying a ligand for a prion protein, the method comprising:
- a) contacting a test agent with a peptide comprising at least three continuous D-amino acids of the sequence D(GGHPQGWWGGHPQGWG) (SEQ ID NO:34); and
  - b) detecting a complex comprising the test agent and said polypeptide, thereby identifying a ligand for a prion protein.
33. The method of claim 32, wherein the peptide comprises at least four continuous D-amino acids of the sequence D(GGHPQGWWGGHPQGWG) (SEQ ID NO:34).
34. The method of claim 32, wherein said test agent is selected from the group consisting of a polypeptide, peptide, peptidomimetic, small organic molecule, small inorganic molecule, nucleic acid, lipid, and a carbohydrate.
35. The method of claim 32, wherein said test agent and polypeptide are contacted in the presence of a metal.
36. The method of claim 35, wherein said metal is copper.
37. The method of claim 36, wherein said copper is present in a concentration of 100 nM to about 500  $\mu$ M.
38. The method of claim 36, wherein said copper is present at a concentration from about 500 nM to about 200  $\mu$ M.
39. A ligand identified according to the method of claim 32.

40. A method of detecting the presence of a prion protein in a biological fluid, the method comprising

a) contacting the biological fluid with the ligand of claim 1 under conditions sufficient to cause formation of a complex between said prion protein, if present, in said biological fluid and said peptide; and

b) detecting said complex,

thereby detecting the presence of a prion protein in said biological fluid.

41. The method of claim 40, wherein said biological fluid is selected from the group consisting of blood, plasma, serum, cerebrospinal fluid, urine, saliva, milk, ductal fluid, tears, and semen.

42. A method of detecting the presence of a prion protein in an environmental sample, the method comprising

a) contacting the environmental sample with the ligand of claim 1 under conditions sufficient to cause formation of a complex between said prion protein, if present, in said sample and said ligand; and

b) detecting said complex,

thereby detecting the presence of a prion protein in said sample.

43. The method of claim 42, wherein said environmental sample comprises the water-soluble extract of a solid environmental sample.

44. The method of claim 43 wherein said environmental sample comprises soil, grass or hay.

45. A method of removing a prion from a biological fluid, the method comprising

- a) contacting the biological fluid with the ligand of claim 1 under conditions sufficient to cause formation of a complex between said prion, if present, in said biological fluid and said ligand; and
  - b) removing said complex from said biological fluid, thereby removing said target from said biological fluid.
46. The method of claim 45, wherein said biological fluid is selected from the group consisting of blood, plasma, serum, cerebrospinal fluid, urine, saliva, milk, ductal fluid, tears, and semen.
47. The method of claim 45, wherein said peptide ligand is coupled to a solid support.
48. A method of removing a prion from an environmental sample, the method comprising
- a) contacting the sample with the ligand of claim 1 under conditions sufficient to cause formation of a complex between said prion, if present, in said biological fluid and said ligand; and
  - b) removing said complex from said environmental sample, thereby removing said prion from said environmental sample.
49. The method of claim 48, wherein said environmental sample is selected from the group consisting of soil, hay, the soluble component of soil, and the soluble component of hay.
50. The method of claim 48, wherein said peptide ligand is coupled to a solid support.
51. A method of treating or retarding the development of a prion-associated pathology in a subject, the method comprising administering to said subject the ligand of claim 1 in an amount sufficient to treat or retard the development of said pathology.
52. The method of claim 51, wherein said subject is a human.

53. The method of claim 51, wherein said pathology is Creutzfeldt-Jakob disease, Gerstmann-Straussler-Scheinker disease, fatal familial insomnia, scrapie, bovine spongiform encephalopathy, transmissible mink encephalopathy, feline spongiform encephalopathy, exotic ungulate encephalopathy and chronic wasting disease.

55. The method of claim 54, wherein the Creutzfeldt-Jakob disease is iatrogenic, new variant, familial, or sporadic Creutzfeldt-Jakob disease.

a) contacting a sample known to or suspected of containing a prion protein with an affinity absorbent comprising the ligand of claim 1 under conditions that allow for the formation of a first complex between said ligand and prion, if present;

b) adding an anti-prion antibody under conditions allowing for formation of a second complex between said first complex and said anti-prion antibody; and

c) detecting said second complex,

thereby detecting said prion.

58. The method of claim 56, wherein said sample is an environmental fluid.

60. The method of claim 56, further comprising concentrating said prion protein in said sample prior to contacting said sample with said absorbent.

61. The method of claim 56, further comprising washing said first complex prior to adding said anti-prion antibody.

62. The method of claim 56, wherein said immunoabsorbent is present on a bead.
63. The method of claim 56, wherein said second complex is detected by chemiluminescence.
64. The method of claim 62, wherein the signal associated with second complex is chemiluminescence.
65. The method of claim 56, wherein the signal associated with said second complex is compared to the level of the signal associated with second complex obtained by incubating said anti-prion antibody in a control solution lacking said sample.
66. The method of claim 56, wherein the signal associated with said second complex is compared to the level of the signal associated with second complex obtained by incubating said sample in a solution lacking said anti-prion antibody.
67. A method of detecting the presence of a prion protein in a biological fluid, the method comprising
- a) contacting the biological fluid with an amino resin under conditions sufficient to cause formation of a complex between said prion protein, if present, in said biological fluid and said resin; and
  - b) detecting said complex, thereby detecting the presence of a prion protein in said biological fluid.
68. The method of claim 67, wherein said biological fluid is selected from the group consisting of blood, plasma, serum, cerebrospinal fluid, urine, saliva, milk, ductal fluid, tears, and semen.
69. A method of detecting the presence of a prion protein in an environmental sample, the method comprising



a) contacting the environmental sample an amino resin under conditions sufficient to cause formation of a complex between said prion protein, if present, in said sample and said amino resin; and

b) detecting said complex,

thereby detecting the presence of a prion protein in said sample.

70. The method of claim 69, wherein said environmental sample comprises the water-soluble portion of a solid environmental sample.

71. The method of claim 70 wherein said environmental sample comprises soil, grass or hay.

72. A method of removing a prion from a biological fluid, the method comprising

a) contacting the biological fluid with an amino resin under conditions sufficient to cause formation of a complex between said prion, if present, in said biological fluid and said amino resin and

b) removing said complex from said biological fluid,  
thereby removing said target from said biological fluid.

73. The method of claim 72, wherein said biological fluid is selected from the group consisting of blood, blood compositions, serum, cerebrospinal fluid, urine, saliva, milk, ductal fluid, tears, and semen.

74. A method of removing a prion from an environmental sample, the method comprising

a) contacting the sample with an amino resin under conditions sufficient to cause formation of a complex between said prion, if present, in said environmental sample and said resin; and

b) removing said complex from said environmental sample,  
thereby removing said prion from said environmental sample.

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75. The method of claim 74, wherein said environmental sample is selected from the group consisting of soil, hay, the soluble component of soil, and the soluble component of hay.

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